CLAIMS

1. A method for producing a polypeptide of interest, which comprises:

(a) cultivating a mutant of a parent *Aspergillus* cell, wherein (i) the mutant comprises a first nucleic acid sequence encoding the polypeptide, and (ii) the mutant produces less of at least one toxin of interest than the parent *Aspergillus* cell when cultured under the same conditions; and

(b) isolating the polypeptide from the culture medium.

2. The method of claim 1, wherein the mutant produces less of the toxin(s) as a consequence of modification of at least one of the genes responsible for the biosynthesis or secretion of the toxin(s).

3. The method of claim 1 or 2, wherein the mutant produces at least about 90% less of said toxin than the parent cell when cultured under the same conditions.

4. The method of any of claims 1-3, wherein the toxin is selected from the group consisting of cyclopiazonic acid, kojic acid, 3-nitropropionic acid, emodin, malformin, aflatoxins, ochratoxins and secalonic acids.

5. The method of any of the preceding claims, wherein the mutant produces less of the cyclopiazonic acid and at least a second toxin than the parent *Aspergillus* cell when cultured under the same conditions.

6. The method of claim 5, wherein the second toxin is kojic acid or an aflatoxin.

7. The method of claim 5 or 6, wherein the mutant further produces less of the 3-nitropropionic acid than the parent *Aspergillus* cell when cultured under the same conditions.

8. The method of any of the preceding claims, wherein the *Aspergillus* cell is selected from the group consisting of the *Aspergillus* subgroups Eurotium, Chaetosartorya, Sclerocleista, Satoia, Neosartorya, Hemicarpenteles, Petromyces, Emericella, and Fenellia.

9. A method of any of the preceding claims, wherein the polypeptide of interest is native to the *Aspergillus* host cell.

10. The method of claim 9, wherein the polypeptide of interest is overexpressed by the *Aspergillus* mutant host cell as compared to the expression by the parent *Aspergillus* host cell when cultured under the same conditions.

11. A method of any of claims 1 to 8, wherein the polypeptide of interest is heterologous to the *Aspergillus* host cell.

12. The method of any of the preceding claims, wherein the polypeptide is selected from the group consisting of a hormone or a precursor form thereof, an enzyme or an enzyme variant or a precursor from thereof, an antibody or a functional fragment thereof, a receptor or a functional fragment thereof, and a reporter.

13. The method of claim 12, wherein the enzyme is selected from the group consisting of aminopeptidase, amylase, carbohydrase, carboxypeptidase, catalase, cellulase, chitinase, cutinase, cyclodextrin glycosyltransferase, deoxyribonuclease, esterase, galactanase, alpha-galactosidase, beta-galactosidase, glucoamylase, alpha-glucosidase, beta-glucosidase, invertase, laccase, lipase, lyase, pectate lyase, mannase, mannosidase, mutanase, oxidase, oxygenase, pectinase, endo-peptidase, exo-peptidase, peroxidase, phytase, polyphenoloxidase, protease, ribonuclease, transglutaminase, and xylanase.

14. A toxin-deficient *Aspergillus* mutant host cell useful for the production of a heterologous polypeptide of interest, which cell has been genetically modified in order to produce less of at least one

toxin as compared to an *Aspergillus* parental cell, when cultured under the same conditions.

15. The mutant cell of claim 14, which comprises a first nucleic acid sequence encoding the polypeptide of interest and a second nucleic acid sequence comprising a modification of at least one of the genes responsible for the biosynthesis or secretion of the toxin.

16. The mutant cell of claim 14 or 15, wherein the cell comprises at least two copies of the first nucleic acid sequence.

17. The mutant cell of any of claims 14-16, wherein the polypeptide of interest is native to the mutant cell.

18. The mutant cell of any of claims 14-16, wherein the polypeptide of interest is heterologous to the mutant cell.

19. The mutant cell of any of claims 13-18, wherein the toxin is selected from the group consisting of cyclopiazonic acid, kojic acid, 3-nitropropionic acid, emodin, malformin, aflatoxins, ochratoxins and secalonic acids.

20. The mutant cell of any of claims 13-19, wherein the toxins include a first toxin which is cyclopiazonic acid and a second toxin which is selected from the group of kojic acid, 3-nitropropionic acid and aflatoxins.

21. A method for obtaining a toxin-deficient *Aspergillus* mutant host cell as defined in any of claims 13 to 20, which cell is deficient in the production of at least one toxin of interest, which method comprises (a) subjecting a parent cell to mutagenesis and (b) screening for mutant cells having a reduced or eliminated production of the toxin(s) of interest.

22. The method of claim 21 in which the mutagenesis is random.

23. The method of claim 22, in which the mutagenesis is specific and conducted to modify a nucleotide sequence involved in and necessary for the production or secretion of the toxin(s) of interest.

24. The method of claim 22, comprising introducing into the *Aspergilllus* host cell a nucleic acid sequence comprising a modification of at least one of the genes responsible for the biosynthesis or secretion of the toxin(s) so as to inactivate said gene(s) under conditions mediating homologous recombination with the corresponding native gene of the host cell resulting in a replacement of the native gene with the inactive modified gene.

25. The method of any of claims 21-24, further comprising introducing into the *Aspergillus* parent host cell a nucleic acid sequence encoding a polypeptide of interest.

26. The method of claim 25, wherein the polypeptide of interest is native to the *Aspergillus* cell.

27. The method of claim 25, wherein the polypeptide of interest is heterologous to the *Aspergillus* cell.

28. A method for obtaining a toxin-deficient *Aspergillus* mutant host cell as defined in any of claims 13-20, which comprises (a) introducing into an *Aspergillus* parent host cell a first nucleic acid sequence encoding a polypeptide of interest and a second nucleic acid sequence comprising a modification of at least one of the genes responsible for the biosynthesis or secretion of at least one toxin; and (b) identifying the mutant from step (a) comprising the nucleic acid sequences.

29. The method of claim 28, further comprising subjecting the *Aspergillus* parent host cell to mutagenesis prior to or after the introduction of the first and second nucleic acid sequences.

30. The method of claim 29, wherein the mutagenesis is achieved by one or more procedures selected from the group consisting of specific or random mutagenesis, PCR generated mutagenesis, site-specific DNA deletion, insertion and/or substitution, gene disruption or replacement techniques and anti-sense techniques.

31. A nucleic acid sequence encoding dimethylallyl-cycloacetoacetyl-L-tryptophan synthase, substantially as depicted in SEQ ID NO: 1.

32. Use of the nucleic acid sequence of claim 31, or an active fragment thereof, for the disruption of similar genes in filamentous fungal host strains.

33. The use of claim 32, wherein the filamentous fungal host strain is selected from the group consisting of *Aspergillus*, *Trichoderma*, *Penicillium* and *Fusarium* spp.

34. An isolated dimethylallyl-cycloacetoacetyl-L-tryptophan synthase obtainable from an *Aspergillus oryzae* strain, selected from the group consisting of:

(a) a dimethylallyl-cycloacetoacetyl-L-tryptophan synthase having substantially the amino acid sequence of SEQ ID NO: 2;

(b) an allelic variant of (a); and

(c) a fragment of (a) or (b), which has dimethylallyl-cycloacetoacetyl-L-tryptophan synthase activity.

35. A mutant *Aspergillus* cell suitable for the expression of heterologous polypeptides, wherein one or more silent toxin genes have been eliminated.

36. The mutant of claim 35, wherein one or more toxin gene(s) have been eliminated by non-revertably detetion or disruption of all or part of the toxin gene(s).

37. The mutant of claim 35 or 36, wherein the *Aspergillus* cell is selected from the group consisting of the *Aspergillus* subgroups

Eurotium, Chaetosartorya, Sclerocleista, Satoia, Neosartorya, Hemicarpenteles, Petromyces, Emericella, and Fenellia.

38. The mutant of any of claims 35-37, wherein the toxin gene(s) encode(s) one or more toxins selected from the group consisting of cyclopiazonic acid, kojic acid, 3-nitropropionic acid, emodin, malformin, aflatoxins, ochratoxins and secalonic acids.

39. The mutant of any of claim 35-38, wherein the toxin gene in question encode an aflatoxin.

40. The mutant of any of claims 35-39, wherein the toxin gene(s) are from the *A. oryzae* aflatoxin cluster, in particular selected from the group comprising omtA, aflR, pksA, Nor-1, fas-beta, fas-alpha, vber-1, avnA, ord-2.

41. The mutant of claim 40, wherein the parent *Aspergillus* cell is an *A. oryzae*, in particular *A. oryzae* A1560 (IFO 0417).

42. The mutant of claim 41, wherein the aflatoxin gene(s) are selected from the group consisting of omtA and aflR.